Cellular Phenotypes in Human iPSC-Derived Neurons from a Genetic Model of Autism Spectrum Disorder.

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Public Summary:

Scientific Abstract:
A deletion or duplication in the 16p11.2 region is associated with neurodevelopmental disorders, including autism spectrum disorder and schizophrenia. In addition to clinical characteristics, carriers of the 16p11.2 copy-number variant (CNV) manifest opposing neuroanatomical phenotypes-e.g., macrocephaly in deletion carriers (16pdel) and microcephaly in duplication carriers (16pdup). Using fibroblasts obtained from 16pdel and 16pdup carriers, we generated induced pluripotent stem cells (iPSCs) and differentiated them into neurons to identify causal cellular mechanisms underlying neurobiological phenotypes. Our study revealed increased soma size and dendrite length in 16pdel neurons and reduced neuronal size and dendrite length in 16pdup neurons. The functional properties of iPSC-derived neurons corroborated aspects of these contrasting morphological differences that may underlie brain size. Interestingly, both 16pdel and 16pdup neurons displayed reduced synaptic density, suggesting that distinct mechanisms may underlie brain size and neuronal connectivity at this locus.